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PCT ORGANISATION MONDIALE I Bureau

WO 9602210A1

EMANDE INTERNATIONALE PUBLIEE EN VERTU DU

(51) Classification internationale des brevets 6 :
A61F 2/06, A61M 31/00

A1

(43) Date de publication internationale: 1er février 1996 (01.02.96)

(21) Numéro de la demande internationale: PCT/FR95/00869

(22) Date de dépôt international: 29 juin 1995 (29.06.95)

(30) Données relatives à la priorité:
94/08933 13 juillet 1994 (13.07.94) FR

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(81) Etats désignés: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ, VN, brevet européen (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), brevet OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), brevet ARIPO (KE, MW, SD, SZ, UG).

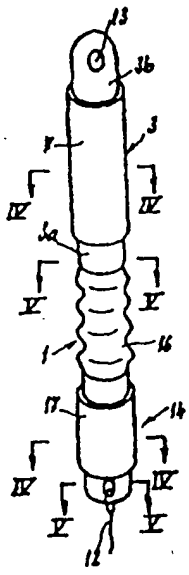
Publiée
*Avec rapport de recherche internationale.*

(54) Title: THERAPEUTIC DEVICE FOR THE SELECTIVE CYTOREDUCTION TREATMENT OF AN OBSTRUCTION IN A NATURAL LUMEN OR PASSAGE OF THE HUMAN OR ANIMAL BODY

(54) Titre: DISPOSITIF THERAPEUTIQUE DESTINE AU TRAITEMENT CYTOREDUCTEUR SELECTIF DE L'OBSTRUCTION D'UNE LUMIERE OU VOIE NATURELLE D'UN CORPS HUMAIN OU ANIMAL

(57) Abstract

Therapeutic device (1) for the selective cytoreduction treatment of an obstruction in a natural lumen or passage (2) of the human or animal body, wherein said lumen is obstructed by the localised proliferation of cells, and said device comprises a normally cylindrical tubular element (3) to be located within said natural lumen, which is flexible enough to conform to said natural lumen but rigid enough to provide an artificial channel (4) within said lumen. The tubular element (3) supports lengthwise a medicinal sleeve (7) for registration and engagement with said obstruction once the tube has been located, and arranged for local delivery, at least in its outer surface portion, of one or more cytoreduction, in particular cytotoxic, therapeutic agents, by contacting the cells obstructing said lumen (2).




(57) Abrégé

Dispositif (1) thérapeutique destiné au traitement cytoréducteur sélectif de l'obstruction d'une lumière ou voie naturelle (2) d'un corps humain ou animal, ladite lumière étant obstruée sous l'effet d'une prolifération cellulaire locale, ledit dispositif comprenant un élément tubulaire (3) destiné à être placé dans ladite lumière naturelle, notamment de forme cylindrique, suffisamment souple pour se conformer à ladite lumière naturelle, mais suffisamment rigide pour maintenir un passage artificiel (4) dans ladite lumière. L'élément tubulaire (3) supporte selon sa longueur un manchon médicamenteux (7), destiné à venir en regard et au contact de l'obstruction une fois la lumière naturelle intubée, et agencé pour délivrer localement, au moins dans sa partie superficielle externe, au moins un agent thérapeutique cytoréducteur, notamment cytotoxique par contact avec les cellules sous l'effet desquelles ladite lumière (2) est obstruée.

# THERAPEUTIC DEVICE FOR SELECTIVE CYTOREDUCTIVE TREATMENT OF THE OBSTRUCTION OF A LUMEN OR A NATURAL OPENING OF A HUMAN OR ANIMAL BODY

This invention concerns the treatment of a lumen or natural opening located in a whole part, especially in a solid organ of a human or animal body, lumen through which there is flow or circulation of fluid, especially a bodily fluid, liquid or gaseous, which lumen or natural opening is obstructed by the effect of a local cellular proliferation.

For example, the urinary system, and in particular the urethra, constitute natural lumens in the sense of this invention.

"Local cellular proliferation" is understood to be any biological process — for example, of benign or malignant tumoral type — leading locally to an excess of tissue, organized or not, and causing an obstruction, or obstructing the lumen or natural opening considered, in the location where said proliferation develops. The benign hypertrophy of the prostate or prostatic adenoma constitutes an example of such obstructive cellular proliferation.

This invention will be introduced, defined and described, as an example without limitation thereto, by reference to the treatment of acute or chronic prostatic obstacles in man.

Today, the prostatic obstacle is treated mechanically, i.e. without curative action concerning the cause of the obstruction and, for this purpose, various endo-urethral prostheses have been described or are available in the market. As an example, reference will be made to the prosthesis described in document WO-A-94/18907.

Such prostheses, implanted permanently or temporarily, give only palliative treatment of prostatic obstacles.

For the patient, these prostheses may be poorly tolerated, due to their purely mechanical action, since they are foreign bodies left in place permanently, or temporarily but repeatedly. In certain cases, there may be a non-negligible risk of infection and migration. When they are permanent, these prostheses present a risk of obstruction, either by encrustation (deposit of crystals contained in urine) or by hyperplasia inside the prosthesis, as a reaction to the foreign body it represents; such hyperplasia can even obstruct certain permanent prostheses.

The object of this invention is to remedy these shortcomings.

More precisely, the object of the invention is a treatment of the obstruction of a natural lumen, limited over time, of a curative type, with local and selective action.

In accordance with this invention, a new device is proposed for therapeutic treatment, implanted in the lumen or natural opening to be treated, including:

- in a manner known *per se*: a tubular, non-biodegradable element, designed to be placed and retained in a mainly autostatic manner, in the natural treated lumen; this element, preferably cylindrical in shape, is both sufficiently flexible to adapt to the natural lumen against its wall and sufficiently rigid to maintain an artificial passage and, therefore, circulation in the natural lumen;

- in a novel sense: a medication tampon, supported by the tubular element, positioned on the length and around the latter in order to come at the level and in direct contact with the obstruction, after the natural lumen is intubated with said tubular element; this tampon includes or incorporates a cytoreductive therapeutic agent, in particular cytotoxic specifically in connection with the cells of said local cellular proliferation, essentially by simple tissue contact, superficial and solid, with said cells; on the other hand, this tampon is designed to deliver such therapeutic agent, at least in its external part.

"Supported by," in accordance with this invention, is understood to mean that the medication tampon is present in the tubular element, being either apparent and/or separate from the latter, or invisible, included or incorporated in said tubular element, in its matter or components, on a predetermined length and/or position of said tubular element.

"Therapeutic," in accordance with this invention, is understood to be any drug-type treatment and in particular chemical, isolated or complementary to another treatment, locally allowing to selectively reduce the obstruction of the lumen or natural opening considered — whether it consists of cells coating the wall of said lumen or cells located behind and in depth, as compared to the latter. This drug-type treatment is facilitated or completed, in accordance with this invention, by mechanical treatment designed to maintain — during treatment — then to reestablish — in the natural lumen — the flow impaired or prevented by the obstruction of said lumen.

Thanks to the invention, after the therapeutic device is placed in the obstructed natural lumen, the medication tampon delivers the cytoreductive agent selectively to the obstructed part of the wall of the natural lumen, and then to the underlying cell proliferation. As a consequence of such delivery, a progressive erosion takes place in the obstructed part of the wall of the natural treated lumen, then in the underlying tissue responsible for the compression or obstruction of the same lumen, on a front shaped as a cylindrical envelope, progressing radially towards the exterior, concentrically to the medication tampon. Thus, a passage is formed through the treated lumen, with a cross dimension at least higher than the normal cross dimension of the same lumen. As soon as the contact stops between the external surface part of the medication tampon and the surrounding tissues or cells, the cytoreductive action stops, with the understanding that it can also stop by simple extraction of the therapeutic device in accordance with the invention, from the natural lumen intubated by it.

Overall, the result is a drug-induced shaping of the natural treated lumen, leaving a passage which is somewhat "molded" over the tubular element of the therapeutic device in accordance with the invention.

Consequently by a twofold effect — both drug-related and mechanical — of the device in accordance with the invention, it is possible to construct a neo-passage in the obstructed part of any natural lumen, generally having the same axis and the same shape as the tubular element which was used to form it. After this neo-passage is created, the device in accordance with the invention is removed, and the neo-channel thus obtained is epithelialized starting from the over and underlying parts of

the natural lumen not treated by the medication tampon.

Preferably, and although this is one method of the embodiment of the invention among others, on the one hand, the tubular element comprises an internal core, for example cylindrical, made of biocompatible material, especially relatively smooth and soft, for example silicon rubber and, on the other part, the medication tampon, which is distinct from the tubular element and covers the latter, is placed inside the core, and includes a biologically compatible substrate or support incorporating the cytoreductive therapeutic agent.

A therapeutic device in accordance with the invention also has the following main advantages.

The cytoreductive therapeutic agent is delivered *in situ* and specifically to the cell proliferation, which generates or generated the obstruction in the natural lumen. Such local administration of a cytoreductive active principle considerably reduces the side effects or morbidity as compared to an administration of the same active principle by a general path, for example, orally, in the case of the treatment of a benign hypertrophy.

The cytoreductive effect is strictly limited to the obstructed part, excluding the surrounding zones of the natural lumen, which remain separated from the action of the cytoreductive therapeutic agent, since the corrosive effect of said agent on the surrounding tissues does not take place other than by mechanical or solid contact, without liquid intermediary. Tissue or cell degradation products are eliminated along the natural lumen from which the obstacle is eliminated. In general, such products or waste can be diluted and evacuated with the bodily fluid circulating in the natural treated lumen.

Tissue or cell degradation products are eliminated through the natural lumen, whereby the obstacle is removed. In general, such products or waste can be diluted and evacuated with the bodily fluid circulating in the natural treated lumen.

A therapeutic device in accordance with the invention can be placed in the treated lumen simply and without trauma.

In the case of the treatment of the prostatic part of the urethra in man, an endo-urethral therapeutic device in accordance with the invention comprises two tubular elements designed to be placed in the urethra, on both sides of the sphincter, respectively, and attached to each other by a connection means, flexible and deformable, designed to be caught in the orifice of the sphincter. The upper tubular element supports the medication tampon in the prostatic part of the urethra and the lower tubular element does not have a medication tampon. In particular, the medication tampon is positioned, in relation to the top tubular element, from a so-called bottom end, located above the lower end (in relation to the implanted position) of the top tubular element, for example at approximately 10 mm from this lower end, to a so-called top end, located behind in relation to the upper end of the top tubular element, for example, at a distance ranging between 10 and 15 mm from this upper end.

For an endo-urethral device, thanks to this complementary location, the cytoreductive effect is limited to the zone of the obstacle which extends from the veru montanum to the neck of the bladder, and especially to the sus-montanal segment of the prostatic urethra.

The part of the top tubular element liable to extend into the bladder after the implant is placed is not dangerous, to the extent that such end, which may come into contact with the wall of the bladder, does not contain cytoreductive agent on a certain length.

An endo-urethral therapeutic device in accordance with the invention is therefore fundamentally different from the endo-urethral device described in document WO-A-89 03232, due to the fact that:

- it allows treating a lumen or anatomic canal, in this case the urethra, which is obstructed, present in a solid or whole organ, in this case the prostate, and not generally an anatomic cavity, in this case the bladder, filled with a liquid serving for the diffusion of the therapeutic agent;
- the support of the therapeutic agent or active principle used is placed along and around the tubular element, and not at the free end of the latter, which, in accordance with this invention, remains without said therapeutic agent;
- the action of the therapeutic agent is exercised by simple tissue contact, superficial and solid with the cells to be destroyed, and not by diffusion in a liquid which, in turn, bathes the wall to be treated; for example, but not exclusively, any therapeutic, non-hydrosoluble agent can be retained in accordance with this invention.

And the therapeutic device in accordance with the invention is fundamentally distinguished from the device described in document EP-A-O 164 241, due to the fact that the tubular element is designed to be autostatic and not free in an anatomic cavity, such as the belly of a ruminant, and to assure inside the circulation of a fluid, and not to contain a biodegradable block in which the therapeutic agent is incorporated.

All these structural and functional differences as compared to the prior state of the art identified above justify in particular the fundamental novation brought by this invention, residing in particular in the notion of drug-induced shaping of a natural canal or lumen in a whole or solid organ, as described and defined above.

This invention is now described by reference to the enclosed drawing, in which:

- figure 1 represents a sagittal anatomic section of the urinary system of the human male body; a therapeutic device in accordance with this invention is represented in this section, in place in the urethra;

- figures 2 and 3 represent a therapeutic device in accordance with this invention, seen from the front, with its upstream end at the top and its downstream end at the bottom, respectively in its configuration before implantation, i.e. ready to be used, and in its configuration after implantation and activation, i.e. in the urethra, whereby the latter is not represented in figure 3;

- figure 4 represents a cross-section of the device represented in figure 2, in accordance with section plane IV-IV, in the top and bottom tubular elements, respectively, before implantation;

- figure 5 represents a cross-section of the device represented in figure 2, in accordance with section plane V-V, taken respectively in the bottom and top tubular elements;

- figure 6 represents a cross-section of the device represented in figure 3, after implantation and activation, in accordance with section plane VI-VI, taken respectively in the bottom and top tubular elements of the device;

- figure 7 represents an actual section of the device represented in figure 3, in accordance with section plane VII-VII, taken respectively in the bottom and top tubular elements of the device;
- figure 8 represents, as in figure 2, another method of embodiment of a device in accordance with the invention;
- figure 9 represents an axial section of the device represented in figure 8 in accordance with section to section plane IX-IX;
- figures 10 and 11 represent an axial section of another method of embodiment of a therapeutic device in accordance with this invention, respectively before implantation and after implantation and activation in the urethra, whereby the latter is not represented;
- figures 12 and 13 represent two cross-sections of a variation of embodiment of a device represented in figure X, before implantation, respectively in accordance with section planes XII-XII and XIII-XIII, identified in figure 10;
- figures 14 and 15 represent cross-sections of the device represented in figures 12 and 13, respectively in accordance with section planes XIV-XIV and XV-XV, identified in figure 11, after implantation and activation;
- for a variation of embodiment of the therapeutic device represented in figures 12 to 15, figures 16 and 17 represent axial sections, respectively in accordance with section planes XII-XII and XIII-XIII, identified in figure 10 before implantation;

- in relation, respectively, to section planes XII-XII and XIII-XIII, identified by reference to figure 10, figures 18 and 19 represent axial sections of another method of embodiment of a therapeutic in accordance with the invention;

-schematically, and in front view, figures 20 to 24 represent the urethra before implantation in accordance with figure 20, the method of action of a therapeutic device in accordance with the invention, implanted in accordance with figures 21 to 23, and the urethra after extraction of said device, in accordance with figure 24;

- figure 25 represents, in position implanted in vivo, a therapeutic device in accordance with the invention, represented with its extraction or anchorage cord;

- figures 26 and 27 represent, in vivo and in cross-section, respectively, in accordance with section planes XII-XII in figure 10 and XIV-XIV in figure 11, another method of embodiment of a therapeutic device in accordance with the invention, before activation of the device in accordance with figure 26, and after activation of the device in accordance with figure 27.

In accordance with figure 1, the urethra tube extends from top to bottom, from the urinary meatus 18 to the neck 19 of the bladder 20. Above the striated sphincter 15, the urethra includes a prostatic part 21, made up of a sus-montanal prostatic segment 210, and a sub-montanal prostatic segment 211, on both sides of the veru montanum 30 of the prostate. Below the sphincter 15, the urethra includes, towards the meatus 18, the membranous segment 221, the bulbar segment, 222, the perineal segment 223 and finally the penile segment 224.

As a consequence of any adenoma developed at the level of the prostatic part, the latter is liable to become obstructed, so that the therapeutic device in accordance with the description below must be introduced in part 21.

In accordance with figures 2 and 3, this endo-urethral therapeutic device 1 includes, in general, two tubular elements 3 and 14, designed to be placed in the urethra 2, respectively on both sides of the sphincter 15, and attached to each other by means of a connection 16, flexible and deformable, consisting of a flexible and elastic tampon, designed to be caught in the orifice of the sphincter 15. The flexible tampon 16 continues the flow with the tubular elements 3 and 14.

The top tubular element 3, designed to be placed and retained in the prostatic part 21 of the urethra, supports and is covered by a medication tampon 7, positioned along and around said tubular element 3. Consequently, when this tubular element 3 is placed in the prostatic part 21 of the urethra, the medication tampon 7 comes to the level of and in direct contact with the prostatic obstruction. This medication tampon 7 includes a cytoreductive therapeutic agent, specifically for the cells of the prostatic cell proliferation, essentially by simple tissue contact, superficial and solid, with said cells. The tampon 7 is also designed, especially concerning its support, to deliver said therapeutic agent in its external, superficial part; such delivery on the surface of the therapeutic agent may be obtained by any appropriate methods, well known to the professional, for example, quasi-instantaneously or preferably in a slow, retarded or progressive manner, by adjusting the nature and/or

composition of the substrate of the medication tampon, used somewhat as a vehicle of the therapeutic agent proper.

The other bottom tubular element 14 does not have any therapeutic tampon and consequently does not contribute to the therapeutic treatment of the urethra below the sphincter.

Tubular elements 3 and 14 — for example, cylindrical in shape — are sufficiently flexible to take the shape of the urethra, in the implanted position, but sufficiently rigid to maintain an artificial passage 4 in the urethra, assuring the circulation of urine.

The therapeutic tampon 7 is positioned in relation to the top tubular element 3, on its length, so that a so-called bottom end is located above the lower end 3a of the top tubular element 3 — for example, at approximately 10 mm from such lower end — and a so-called top end is located behind and below the upper end 3b of the top tubular element 3 — for example, at a distance ranging between 10 and 15 mm from the aforementioned lower end.

As shown in figures 2 and 3, the upper end of the top tubular element 3 is recessed and perforated 13 to assure the passage of urine from the bladder 20.

Tubular elements 3 and 14 include each a core 6, in the form of a tube made of biocompatible material, but not biodegradable, in particular relatively smooth and soft, for example silicon rubber.

The medication tampon 7 covers the internal core 6 of the top tubular element 4 and is placed outside the latter. This tampon 7 includes a biologically compatible substrate incorporating the cytoreductive therapeutic agent. This substrate can expand and possibly compress radially, so that, when dry and before the device is implanted, it has a condensed, compact, not expanded, shape, and after implantation and activation, when wet or humid, it takes an expanded shape; these two shapes, not expanded and expanded, respectively, are represented in figures 2 and 4, respectively, and 3 and 6. The substrate of the tampon 7 is, for example, a hydrophilic material which expands under the effect of the biological fluids present or circulating in the urethra. As an example of such an expansible and hydrophilic substrate, it is possible to retain various cellulose materials, already used in medicine.

Similarly, but without cytoreductive agent, the bottom tubular element 14 supports and is surrounded by an external cuff 17, covering the internal core 6 of said element 14, expansible and possibly compressible radially, for example, of the same hydrophilic and expansible matter, and possibly biodegradable, as the material used in the composition of the medication.

In the beginning, i.e. before the implantation of the device, the medication tampon 7 is covered by a superficial protective envelope 11, destructible and/or biodegradable by *in situ* tissue contact with the obstructed part of the canal of the urethra. More precisely, this envelope 11 is liable to retain, when not expanded, the medication tampon 7, before the implantation of the device, and then being destroyed, allowing for the totally free

expansion of the tampon 7; this is represented, respectively, in figures 2 and 4 and 3 and 6. Exactly in the same way, a superficial destructible protective envelope 11 can be used to contain, then release the external expansible cuff 17 surrounding the bottom tubular element 14.

As shown in figures 2 and 3, but also in figure 25, an extraction or anchorage cord 12 is anchored to the upstream end of the device, and more precisely to the lower end of the bottom tubular element 14. The upstream end of the cord 12 can also be equipped with a viewing hole 50, for example, a bead anchored on the cord 12, as shown in figure 25.

The medication tampon 7 can incorporate, in addition to the cytoreductive agent, a bacteriostatic agent and possibly all other agents necessary for therapeutic or operative intervention, for example, an X-ray opacifying agent. Preferably, but not exclusively, the cytoreductive agent is chosen among antimitotic, cytolytic agents, enzymes, hormones, anti-enzymes and metallic salts, for example silver salts.

The therapeutic device represented in figures 8 and 9 is different from that represented by reference to figures 2 to 7, by the fact that the tampons 7 and 17 are merged with tubular elements 3 and 14, respectively, and more precisely their core 6, as defined above.

The medication tampon 7 is obtained by direct incorporation at least on the surface of the cytoreductive therapeutic agent in the material, for example, silicon tampon, of the core 6 and of the tubular element 3, in a biologically active extended zone 5, embodied or not.

The superficial protective envelope 11 is, however, kept so as to prevent the release of the cytoreductive agent in the entire part of the therapeutic device, without contact with the obstacle, protruding inside the bladder, for example.

The therapeutic device represented in figures 10 and 11 is different from that represented in figures 2 and 7, by the fact that:

- the substrate of the medication tampon 7, in its non-radially expanded configuration, presents an external surface inscribed in the rest of the external surface of the top tubular element 3; and in the expanded position, represented in figure 11, the external surface of the medication tampon 7 protrudes from the external surface of the same tubular element 3;
- the same configuration, not expanded, then expanded, is retained from the external cuff 17 of the bottom tubular element 14.

The therapeutic device represented in figures 12 to 15 is different from that represented by reference to figures 2 to 7, by the fact that the medication tampon 7 is limited to a superficial, cylindrical layer of the substrate, while the rest of the latter constitutes a connection tampon 7, expansible, intercalated between the core 6 of the tubular element 3 and the medication tampon 7 proper. The bottom tubular element 14 remains unchanged.

The therapeutic device represented in figures 16 and 17 is not different from that represented by reference to figures 12 to 15, other than by the fact that the medication tampon 7, but also the connection tampon 10, both expansible, include several radial passages 9 from the exterior to the interior of the substrate, so as to allow and favor the passage of bodily liquids or secretions,

contributing or increasing the expansion of the hydrophilic matter. These radial passages are also made in the superficial protective envelope 11, as well as in the top tubular element 3 and in the bottom tubular element 14.

The therapeutic device represented by reference to figures 18 and 19 does not differ from that represented by reference to figures 12 to 15 other than by the fact that it includes a sheath 8 made of synthetic foam, both compressible and expansible radially, between the medication tampon 7 proper and the core 6 of the top tubular element 3. Except for the medication tampon 7, the same configuration is retained for the external cuff 17 of the bottom tubular element 14.

A therapeutic device 1, in accordance with this invention, can be implanted in the urethra 2 exactly in the same fashion as described in document WO-A-04/18907, and in particular with the insertion, assemblies or systems described in said document. These non-traumatic insertion means or devices are removed as soon as the therapeutic device, in accordance with this invention, is inserted in the urethra.

Starting from the urethra schematically represented before implantation in accordance with figure 20, and from a therapeutic device in accordance with the invention as shown in figures 2 to 7, the therapeutic treatment of prostatic adenoma is obtained in the following manner:

After non-traumatic incision, the therapeutic device 1 is positioned in relation to the sphincter 15 by simple traction of the anchorage cord 11. The control of the correct position of the therapeutic device may be obtained endo-rectal echography. The result is the position represented in figure 21.

When in contact with natural secretions, the therapeutic device is activated, and the superficial envelope 11 covering the medication tampon 7 is destroyed in direct contact with the urethra, so that the urethra, then the adenoma, are then in direct contact with the external surface of said tampon 7. The same occurs in relation to the bottom tampon 17.

At that time, tampons 7 and 17 expand in all their lengths, simultaneously, at the level of the bottom tubular element 14 and top element 3. This expansion of the tampon 7 increases the contact surface between the latter and the prostatic urethra, at the same time with pressure at the level of the adenoma behind the urethral mucosa. The expansion of the tampon 17 increases its section in the bulbourethra, and improves the longitudinal stability or autostatism of the therapeutic device in accordance with this invention.

Thus, the result is the configuration of the device represented *in situ* in figure 22.

Gradually, the erosion of the urethra 2, then of the adenoma, progresses, in accordance with a mainly cylindrical surface front, centered on the medication tampon 7 while the mechanical contact with the external surface of the medication tampon 7 allows the cytoreductive agent to exercise its chemical effect on the surrounding tissues. As soon as the erosion progressed to lead to a cavity with a cross-section mostly equal to that of the tampon 7, the contact between the cytoreductive agent and the tissues disappears, and the therapeutic effect stops.

As of that time, urine easily flows between the tampon 7 and the tissues, impregnating the hydrophilic substrate, which can also be biodegradable, for example, by the effect of a modification of urinary pH. The same degradation is observed for tampon 17. As of that time, the

hydrophilic substrate is destroyed, leading to the configuration represented in figure 23.

Finally, the therapeutic device can be removed, as soon as one wishes to interrupt the therapeutic effect, or when the latter has become nonexistent, due to the absence of contact between the tissues and the medication tampon 7. The removal of the device 1 is possible by simple traction on the anchorage cord 12, with the result that the urethra is fully treated in accordance with figure 24.

If one uses a device in accordance with figures 8 and 9, the expansion phase is eliminated.

If one uses a device in accordance with figures 18 and 19, the resorption phase of tampons 7 and 17 is eliminated.

The utilization of a therapeutic device in accordance with the invention, brings great safety, both passive and active.

In connection with passive safety, concerning the bladder 20, there is no direct contact between the medication tampon 7 and the wall of the bladder. Supposing that part of the tampon 7 emerges into the bladder and bathes in urine, in the absence of rubbing with tissues, the protective envelope 11 will not be destroyed or degraded, which prevents the release of cytoreductive agents; by being deposited on this envelope, the salts contained in urine form an additional protective layer. In connection with passive safety at the level of the sphincter, it will be noted in accordance with the above description, that the latter is more than 10 mm away from the medication tampon 7. The sub-montanal segment 211 is not intubated by the medication tampon 7, and represents a safety barrier for the sphincter 15. The bulbourethra.

is never in contact with the medication tampon 7, except for a second at the time of insertion of the device 1. The cytoreductive effect cannot exceed in depth the prostate since, as indicated above, the effect is by contact; contact is limited in depth by the section of the medication tampon 7, in its expanded configuration.

In connection with active safety, the means to control the correct position of device 1 are:

- for the physician, at the time of implantation or during a checkup, endo-rectal and supra-pubic echography, for example; later, the degree of resorption can be evaluated by measuring the diameter of the medication tampon, using an X-ray;
- for the patient, the cord 12 and its bead 50, which comes out at the level of the meatus 18, allowing the patient to check whether the device is in the correct position, with each urination; its disappearance may make him fear a migration upwards, which imposes rapid medical control, while its migration downwards will cause dysuria or urine leakage also imposing medical control;

Finally, the cord 12 has a triple role:

- positioning of the device immediately after insertion;
- proof of the correct position of the device throughout the duration of the treatment;
- and a means to extract the device at the end of the treatment.

Any infection may be prevented by incorporating a bacteriostatic agent in the medication tampon 7.

A device in accordance with the invention also offers optimal cost-efficacy ratio, for the following reasons.

The treatment does not require any heavy external instrumentation, since it can be installed without general anesthesia, with a simple contact anesthetic gel in the urethra. And a simple endo-rectal echography allows controlling the correct position of the therapeutic device.

The morbidity of the therapeutic device is much lower than surgery, and is reduced to perineal discomfort and transitory aggravation of prostatism. But, in any case, morbidity will be limited to the time necessary for the action of the therapeutic device, since the latter is installed temporarily.

In terms of efficacy, with a device in accordance with the invention, a cavity with the appropriate shape is created, for example, cylindrical, inside the prostate, with a result close to that which can be obtained by surgery.

Overall, in accordance with the invention, maximum efficacy (of surgery) is successfully combined with minimal morbidity (of a drug) for a limited cost (the cost of a prosthesis).

In accordance with this invention, the therapeutic device can have a single size, since a length of the top tubular element on the order of 70 mm allows treating most prostatic obstacles.

The medication tampon can incorporate non-cytostatic or cytolytic chemical compounds, such as alpha-blockers, enzymatic inhibitors, enzymes or hormones, in order to reduce exposure of the entire body to these therapeutic agents and reduce their morbidity while conserving satisfactory efficacy.

In accordance with figures 26 and 27, the axis of the medication tampon 7 and the axis of the internal core 6 are offset, so as to destroy proliferating cells in the direction of choice.

A therapeutic device in accordance with the invention also has the following advantages:

- the flexible connection tampon 16 between tubular elements 3 and 14 can have holes, distributed around its contour, especially by longitudinal slots or windows;
- tubular elements 3 and 14 form with the tampon 16, in its flow configuration, conduit with mainly constant internal section in the longitudinal direction of the device;
- the wall of each tubular element 3 or 14 and, in particular, its core 6, have a tubular armature, specifically a metallic or non-metallic spiral, for example submerged in the material of each element.

CLAIMS

1/ Therapeutic device (1), designed for the local and selective treatment of the obstruction of a lumen or natural opening (2) for the circulation of a fluid, located in a whole part, especially in a solid organ of a human or animal body, which lumen or natural opening is obstructed by the effect of a local cellular proliferation, **characterized by the fact** that it consists of:

- a tubular, non-biodegradable element (3), designed to be placed and retained in a mainly autostatic manner, in said natural lumen, mainly cylindrical in shape, sufficiently flexible to adapt to the natural lumen against its wall, but sufficiently rigid to maintain an artificial passage (4) in said lumen;
- a medication tampon (7), supported by said tubular element (3), positioned on the length and around the latter in order to come at the level and in direct contact with the obstruction, after the natural lumen is intubated with said tubular element, including a cytoreductive therapeutic agent, in particular cytotoxic specifically in connection with the cells of said local cellular proliferation, essentially by simple tissue contact, superficial and solid, with said cells, and designed to deliver such therapeutic agent, at least in its superficial external part.

2/ Therapeutic device in accordance with claim 1, characterized by the fact that the medication tampon (5) is incorporated into the tubular element (3).

3/ Therapeutic device in accordance with claim 2, characterized by the fact that the tubular element (3) comprises a core (6) made of biocompatible material, especially relatively smooth and soft — for example, silicon rubber and placed in

a biologically active zone (5) of said tubular element corresponding to said medication tampon (7), whereby the material of the core (6) incorporates the cytoreductive therapeutic agent, at least on the surface.

4/ Therapeutic device in accordance with claim 1, characterized by the fact that the medication tampon (7) is distinct from the tubular element (3) and covers the latter.

5/ Therapeutic device in accordance with claim 4, characterized by the fact that, on the one hand, the tubular element (3) comprises an internal core (6) made of biocompatible material, especially relatively smooth and soft — for example, silicon rubber — and, on the other part, the medication tampon (7) found outside the core (6) includes a biologically compatible substrate incorporating the cytoreductive therapeutic agent.

6/ Therapeutic device in accordance with claim 5, characterized by the fact that the substrate of the medication tampon (7) expands radially, especially so that the external surface of said tampon can, in particular, be inserted, in non-expanded configuration, into the rest of the external surface of the tubular element (3); and in the expanded position, it can protrude from the external surface of the same tubular element.

7/ Therapeutic device in accordance with claim 6, characterized by the fact that the substrate of the medication tampon (7) is hydrophilic and expands under the effect of the biological fluids present or circulating in the obstructed natural lumen.

8/ Therapeutic device in accordance with claim 6, characterized by the fact that it includes a sheath (8) made of synthetic foam, connecting the medication tampon (7) and the core (6) of

the tubular element (3).

9/ Therapeutic device in accordance with claim 5, characterized by the fact that the medication tampon (7) includes several radial passages (9) from the exterior to the interior of said medication tampon (7).

10/ Therapeutic device in accordance with claim 5, characterized by the fact that it includes a connection tampon (10), expansible, intercalated between the core (6) of the tubular element (3) and the medication tampon (7).

11/ Therapeutic device in accordance with claim 1, characterized by the fact that it includes a superficial envelope (11) which protects the medication tampon (7), biodegradable by *in situ* tissue contact with the obstructed part of the natural lumen or canal.

12/ Therapeutic device in accordance with claim 1, characterized by the fact that an extraction cord (12) is anchored to the upstream end (in relation to the implantation direction) of the tubular element (3).

13/ Therapeutic device in accordance with claim 1, characterized by the fact that the medication tampon (7) incorporates a bacteriostatic agent and possibly an X-ray opacifying agent.

14/ Therapeutic device in accordance with claim 1, characterized by the fact that the cytoreductive agent is chosen among antimitotic, cytolytic agents, enzymes, hormones, anti-enzymes and metallic salts.

15/ Therapeutic device in accordance with claim 5, characterized by the fact that the axis of the medication tampon (7) and the axis of the internal core (6) are offset.

16/ Therapeutic device in accordance with any of the claims 1 through 15, designed for the treatment of the prostatic part (21) of the urethra in man, characterized by the fact that the medication tampon (7) is positioned, in relation to the tubular element (3), from a so-called bottom end, located above the lower end (3a) of said tubular element (3), for example at approximately 10 mm from said lower end, to a so-called top end, located behind in relation to the upper end of the top tubular element (3b) — for example, at a distance ranging between 10 and 15 mm from said upper end.

17/ Therapeutic device in accordance with claim 16, characterized by the fact that the upper end (3b) of the tubular element is recessed and perforated (13) to assure the passage of urine from the bladder.

18/ Therapeutic device in accordance with claim 16, characterized by the fact that it comprises two tubular elements (3, 14), designed to be placed in the urethra (2), on both sides of the sphincter (15), respectively, and attached to each other by a connection means (16), flexible and deformable, designed to be caught in the orifice of the sphincter, and the upper tubular element (3) supports the medication tampon (7) in the prostatic part (21) of the urethra, and the other lower tubular element (14) does not have a medication tampon.

19/ Therapeutic device in accordance with claim 18, characterized by the fact that the bottom tubular element (14) comprises a core (6), made of biocompatible but non-biodegradable material, especially relatively smooth and soft — for example, silicon rubber.

20/ Therapeutic device in accordance with claim 18, characterized by the fact that the bottom tubular element (14) includes an external cuff (17), expansible radially, specifically so that the external surface of said external cuff, in non-expanded position, can be inserted into the rest of the external surface of the bottom element (14) and, in expanded position, emerge from the external surface of said bottom element.